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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/697,863	10/30/2003	David E. Clapham	110313.135US3	1595
23483	7590	06/29/2009		
WILMERHALE/BOSTON 60 STATE STREET BOSTON, MA 02109			EXAMINER WEGERT, SANDRA L	
			ART UNIT 1647	PAPER NUMBER
			NOTIFICATION DATE 06/29/2009	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/697,863	Applicant(s) CLAPHAM ET AL.	
	Examiner SANDRA WEGERT	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 March 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-6 and 8-25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-6 and 8-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 October 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>3/4/09</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application, Amendments, and/or Claims

The Information Disclosure Statement, sent 4 March 2009, is acknowledged and entered. There is no record of this IDS being submitted previously (as per Remarks, p. 13). Applicants' request for reconsideration and the Remarks, submitted 4 March 2009, are acknowledged. Claims 2, 7 and 26-111 have been cancelled. Claims 1, 3-6 and 8-25 are pending in the instant application.

Claims 1, 3-6 and 8-25 are under examination in the instant Office Action.

Withdrawn Objections/Rejections

Claim Rejections- 35 USC § 102

The following are quotations of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claim 12 under 35 U.S.C. 102(b) for being unpatentable over Hillier, et al (1997, Accession No. AA416682.1) is *withdrawn*. Hillier, et al disclose a polynucleotide sequence encoding a calcium channel which is 19.3% identical to SEQ ID NO: 1 in the instant application and 99% identical from residues 1592 to 2056 of SEQ ID NO: 1. Applicants pointed out that claim 12 recites a kit, which includes a means of

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detecting the nucleic acid (4 March 2009, p. 11 and 12). Hillier, et al disclose only the nucleic acid sequence and not a means of detection.

Maintained Objections and/or Rejections

Claim Rejections-35 USC § 112, first paragraph, Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1, 3-6 and 8-25, under 35 U.S.C. § 112-1st paragraph, for improper breadth, is *maintained*. The reasons for this rejection were laid out in the previous Office Action (4 December 2008, pp. 4 and 5). Simply put, the specification enables use of the full-length nucleic acid of SEQ ID NO: 1, but does not reasonably provide enablement for *variants, fragments, or epitopes* of SEQ ID NO: 1, or of nucleic acids encoding polypeptides having at least *80% sequence identity* to SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims.

Applicants are not enabled for *fragments* or *variants* of polynucleotides: 1) at least 10-18 consecutive bases long, 2) identified by substructures of the encoded protein (such as a transmembrane domain), 3) encoding "at least an epitope" of a CatSper1

protein, 4) having at least 80% sequence identity, or 5) that hybridize to the claimed nucleic acids at low or moderate stringency, as recited in Claims 1, 3-6, 8, 10 and 11, and embraced by claims 1, 3-6 and 8-25.

Applicants discuss the legal requirements for enablement, with which the examiner agrees (Remarks, p. 6, 4 March 2009), and cite the case of the United States v. Teletronics, Inc. (857 F.2d 778, 785, USPQ2d 1217, 1223 (Fed. Cir. 1988)). U.S. v. Teletronics sets forth the amount of further experimentation needed to enable the claimed invention. The application under review in that case involved the use of steel electrodes, the use of which may not have required as much experimentation as a variant of a channel. Nevertheless, the case has been interpreted to mean that a claimed invention is enabled if any person skilled in the art can make and use the invention without undue experimentation. Such is not the case in the instant application: applicants have not made or tested *any* of the claimed variants of SEQ ID NO: 1, or the encoded polypeptide of SEQ ID NO: 2, and then *tested* them to ensure that they encoded a CatSper1 channel. Nor have applicants provided guidance as to what residues can be changed in the channel or gene without disrupting the function of SEQ ID NO: 1 or the encoded polypeptide.

Applicants' arguments concerning the enablement of variants and fragments of SEQ ID NO: 1 are based on the Utility of the CatSper nucleic acid and also on the fact that one could easily produce short fragments of nucleic acid or polypeptide (Remarks, 3 March 2009, p. 7). However, even with a known utility for the full-length SEQ ID NO: 1, applicants have not demonstrated how any *fragments* or *variants* of SEQ ID NO: 1 can be used. All data presented in the instant Specification concern only the full-length

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nucleic acid of SEQ ID NO: 1. As to whether one can *make* fragments or variants of a nucleic acid or polypeptide, the examiner agrees that one of skill in the art can easily make fragments and variants of an encoded polypeptide. However, applicants have not demonstrated that such fragments and variants fall into the genus of molecules that would be considered a CatSper channel. Furthermore, the broad brush discussion of making and screening for variants does not constitute adequate guidance to practice the claimed method, but rather constitutes an invitation to experiment empirically.

As far as applicant's discussion of the Nikpoor et al reference discussed previously (for example, in the Office Action of 12/04/2008), the examiner agrees that the reference provides *Utility* to the instant claimed invention. However, it does not address the question of enablement of the invention as claimed. In it, the authors discuss the role of the CatSper channel in mice and human patients, and they measure gene expression using PCR. However, the instant claims are to hybridizing fragments, which are not useful in a study such as that shown in the paper, simply because they can vary substantially from the parent sequence. Thus, a similar study performed with the claimed fragments would not accurately and exclusively detect expression of the CatSper1 channel of SEQ ID NO: 1. Hence, the fragments are not enabled as claimed.

Applicants also argued that the chance of a length of nucleic acid, even 10 bases long, binding to a gene other than CatSper1 is essentially zero, and that this therefore means that the recited short fragments are enabled (Remarks, p. 8). However, applicants are assuming very high stringency binding, and the claims either do not recite stringency conditions, or they recite moderate stringency conditions (as in claim 10). Such low or

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moderate stringency conditions means that the nucleic acid "probes" recited will no doubt pick up CatSper1 nucleic acids, as well as many other genes.

35 USC § 112, first paragraph - Written Description.

The rejection of Claims 1, 3-6, 8, 10 and 11 under 35 U.S.C. 112, first paragraph-written description- is *maintained*. The reasons for this rejection based on fragments and homology variants of SEQ ID NO: 1 were set forth at pages 5 and 6 of the previous Office Action (4 December 2009). Applicants did not amend claims referring to non-specific fragments, such as "at least 10 consecutive nucleotides" or "having at least 80% sequence identity." Applicants also did not cancel language referring to variants identified by substructures of the encoded protein (such as the transmembrane domain of the encoded polypeptide, or residues 447-468), or nucleic acids that hybridize to the claimed nucleic acid at only moderate stringency (i.e., a wash step of 65° C). Applicants have neither made nor used *any* variants of SEQ ID NO: 1 or its encoded polypeptide. Therefore applicants were not in possession of all or even a significant number of variants of SEQ ID NO: 1 such that a genus is established. Applicants must have invented the subject matter that is claimed, and furthermore must be in "possession" of what is claimed (Federal Register, 2001, Vol. 66, No. 4, pages 1099-1111, esp. page 1104, 3rd column).

Applicants argue that one of skill in the art can identify sequences with 80% identity to SEQ ID NO: 1, or to any subsequence thereof (Remarks, p. 14). However, being able to *identify* sequences that are variants or fragments is not the same as being in *possession* of variant sequences at the time of filing. Applicants have not described or

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shown possession of a commensurate number of species of compounds that are 80% homologous to Catsper1 or that are variants of Catsper1, and still considered CatSper1 (i.e., have the same function). Alternatively, the applicants could have described and used a representative number of species to demonstrate that they are in possession of a genus of Catsper1 variants that function in the same way as SEQ ID NO: 1. However, applicants have not demonstrated that they can make any functional fragments or variants belonging to the Catsper1 genus.

Claim Rejections- 35 USC § 102

The rejection of Claim 10 under 35 U.S.C. 102(b) for being unpatentable over Sanger Centre (1998, Science, 282: 2012-2018, Accession No. Z82256.1) is *maintained*. The Sanger Centre Consortium discloses a polynucleotide sequence encoding a nematode sodium channel which is 29% identical to SEQ ID NO: 1 in the instant application. There are several short identical areas where the nucleotides are the same, such as in the region of residues 174-181. This reference meets the limitations of claim 10 which recites “at least *a portion* of SEQ ID NO: 1,” as well as hybridization steps that are not stringent (i.e., washing at 65°C).

Applicants argue that the Sanger Centre reference does not teach each and every element embraced by claim 10 (4 March 2009, p. 11). However, the authors did indeed join the disclosed sequence to regulatory sequences in the form of commercial and non-commercial vectors. The paper discusses such cosmid throughout the paper, but see especially p. 2012, column 2 where they introduce the methods used.

The rejection of claims 1, 3 and 8 under 35 U.S.C. 102(b) as being unpatentable over Hillier, et al (1997, Accession No. AA416682.1, see alignment in Appendix A below) in *maintained*. Hillier, et al disclose a polynucleotide sequence encoding a calcium channel which is 19.3% identical to SEQ ID NO: 1 in the instant application and 99% identical from residues 1592 to 2056 of SEQ ID NO: 1. This reference sequence meets the limitations of claims 1, 3 and 8 which recite, respectively: at least 10-18 consecutive nucleotides; a sequence encoding a transmembrane loop (specifically the alpha helix as described in the reference); a sequence that hybridizes to at least 10 consecutive nucleotides of SEQ ID NO: 1; and a portion of the nucleic acids described in any of claims 1, 3-6 and 8-11.

Applicants argue that the Hillier, et al reference does not teach each and every element embraced by claims 1, 3, 8 and 12 (4 March 2009, p. 12). The examiner agrees that the reference does not teach the kit and means of detection recited in claim 12. However, claims 1, 3 and 8 of the instant application simply recite or encompass nucleic acid fragments, the same examples of which are also found in the sequence disclosed in Hiller, et al.

Conclusion: Claims 1, 3-6 and 8-25 are rejected for the reasons recited above.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

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TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Manjunath Rao, can be reached at (571) 272-0939.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business

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Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO

Customer Service Representative or access to the automated information system, call

800-786-9199 (in USA or CANADA) or 571-272-1000.

SLW

20 June 2009

/Bridget E Bunner/
Primary Examiner, Art Unit 1647